Citation:

Lajous M, Willett W, Lazcano-Ponce E, Sanchez-Zamorano L, Hernandez-Avila M, Romieu I. Glycemic load, glycemic index, and the risk of breast cancer among Mexican women. *Cancer Causes Control.* 2005;16:1165-1169.

PubMed ID: 16215866

Study Design:

Population-based Case Control Study

Class:

C - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this study was to compare dietary glycemic load and overall glycemic index with breast cancer risk in Mexican women.

Inclusion Criteria:

- Women whose biopsy confirmed the diagnosis of breast cancer
- Women who agreed to participate and provide dietary information
- Control group was an age-stratified random sample of metropolitan Mexico City residents initially identified using the National Household Sampling Frame

Exclusion Criteria:

No exclusion criteria was reported.

Description of Study Protocol:

Recruitment Cases were interviewed at the six study hospitals before breast cancer was confirmed. Control group was initially recruited using the National Household Sampling Frame.

Design: Case-Control Study

Blinding used (if applicable): not applicable

Intervention (if applicable): not applicable

Statistical Analysis

- Glycemic load and glycemic index were categorized as quartiles among the controls and

relative risk for breast cancer was determined by comparison to the lowest quartile.
- Data were stratified by menopausal status because hormonal status may impact glycemic index and glycemic load
- Analysis was repeated on sub-sample of study population with BMI data available.
- Trend was tested using quartile median values applied to all subjects as continuous variables for dietary glycemic load and glycemic index.

Data Collection Summary:

Timing of Measurements:

From 1990 - 1995, women whose biopsy confirmed the diagnosis of breast cancer were included in the study.

Dependent Variables

- Breast cancer (confirmed by biopsy)

Independent Variables

- Glycemic load for each food calculated by multiplying the carbohydrate content of one serving by the food's glycemic index (obtained from international tables)
- Dietary glycemic load - calculated by summing the product of the food's GL multiplied by the frequency of consumption
- Overall glycemic index - estimated by dividing the dietary glycemic load by the amount of carbohydrates consumed
- Dietary glycemic load and overall glycemic index was obtained for each subject using a validated food frequency questionnaire for Mexicans.

Control Variables

- Age
- Total caloric intake
- Total folate intake
- Socioeconomic status
- Family breast cancer
- Menopausal status
- Parity
- BMI: participants were sent to a health center for anthropometric measurements. BMI was available for only 48% of cases and 50% of controls

Description of Actual Data Sample:

Initial N: 537 eligible cases with breast cancer identified; 1534 eligible controls

Attrition (final N): 475 cases with breast cancer; 1391 controls. 88% of cases and 90% of controls agreed to participate and provide dietary information.

Age:

- <40 years: 16% of cases, 25% of controls
- 40 - 49 years: 24% of cases, 27% of controls
- 50 - 59 years: 27% of cases, 22% of controls
- >60 years: 33% of cases, 26% of controls

Ethnicity: assumed Hispanic

Other relevant demographics: SES, age at first birth, parity, menopausal status and family history.

Anthropometrics: BMI was available for only 48% of cases and 50% of controls

Location: Mexico City, Mexico

Summary of Results:

Odds Ratio (95%CI) of breast cancer according to quartiles of energy-adjusted glycemic load and energy-adjusted overall glycemic index

	Quartile of Intake				
	Q 1	Q 2	Q 3	Q 4	p -trend
All women					
Glycemic Load					
Cases	127	116	77	155	
Controls	339	348	348	348	
Age-adjusted risk	1.00	0.97 (0.71-1.32)	0.66 (0.48-0.91)	1.25 (0.95-1.66)	0.29
Multivariable-adjusted risk*	1.00	1.12 (0.19-1.59	0.83 (0.58-1.21)	1.62 (1.13-2.32)	0.02
Glycemic Index					
Cases	126	89	125	135	
Controls	347	349	347	348	
Age-adjusted risk	1.00	0.69 (0.50-0.94)	1.10 (0.82-1.490	1.04 (0.70-1.37)	0.17
Multivariable-adjusted risk*	1.00	0.61 (0.44-0.84)	1.05 (0.76-1.45)	0.84 (0.62-1.15) 0.81	0.81
Premenopausal women					
Glycemic load					
Cases	62	42	30	55	
Controls	160	164	163	197	

Age-adjusted risk	1.00	0.74 (0.45-1.21)	0.57 (0.35-0.93)	0.87 (0.57-1.32)	0.34
Multivariable-adjusted risk**	1.00	0.94 (0.54-1.63)	0.88 (0.49-1.59)	1.43 (0.81-2.53)	0.24
Glycemic index					
Cases	44	39	50	56	
Controls	164	186	160	176	
Age-adjusted risk	1.00	0.68 (0.42-1.11)	1.32 (0.82-2.14)	1.00 (0.64-1.56)	0.24
Multivariable-adjusted risk**	1.00	0.68 (0.41-1.14)	1.17 (0.71-1.93)	0.66 (0.39-1.12)	0.72
Postmenopausal women					
Glycemic load					
Cases	65	74	47	100	
Controls	185	184	185	151	
Age-adjusted risk	1.00	1.26 (0.83-1.90)	0.81 (0.53-1.25)	1.88 (1.28-2.76)	0.006
Multivariable-adjusted risk**	1.00	1.51 (0.95-2.40)	1.02 (0.62-1.67)	2.18 (1.34-3.55)	0.005
Glycemic index					
Cases	82	50	75	79	
Controls	183	163	187	172	
Age-adjusted risk	1.00	0.68 (0.45-1.02)	0.94 (0.64-1.39)	1.02 (0.71-1.46)	0.59
Multivariable-adjusted risk**	1.00	0.53 (0.35-0.83)	1.07 (0.70-1.64)	0.81 (0.54-1.22)	0.91

*Adjusted for age, total caloric intake, total folate intake, socioeconomic status, family breast cancer, menopausal status, parity and availability of BMI

**Adjusted for age, total caloric intake, total folate intake, socioeconomic status, family breast cancer, parity and availability of BMI

- The multivariate adjusted or for all women comparing the highest quartile of dietary glycemic load with the lowest quartile was 1.62 (95% CI 1.13-2.32; p-test for trend =0.02). This suggests breast cancer risk increases with increasing dietary glycemic load
- No association was observed for overall glycemic index

Other Findings

- An increase in the risk of breast cancer was observed with increasing daily servings of white bread, common biscuit and atole (maize porridge) with milk
- This association was stronger in postmenopausal women indicated by multivariate adjusted OR of 2.18 (95% CI 1.34-3.55; p-test for trend=0.005)
- Premenopausal women had a significantly higher average fiber intake (28.5 g/day) compared to postmenopausal women (25.1 g/day)

- BMI was not found to be a confounder in the relationship between glycemic load and glycemic index and breast cancer

Author Conclusion:

This population-based case-control study of Mexican women showed a direct association between dietary glycemic load and the risk of breast cancer, and this association appeared to be stronger among postmenopausal women. The lack of association observed with overall glycemic index may suggest that intake of rapidly absorbed carbohydrates is a better measure of physiologic response than the proportion of foods with high glycemic index in the diet. High intake of rapidly absorbed carbohydrate appears to play an important role in the risk of breast cancer in Mexican women.

Reviewer Comments:

Authors note the following limitations:

- *Reliance on the applicability of international glycemic index values to the population; glycemic index values were available for 84% of the foods in the FFQ*
- *Hormone use and physical activity are limited in this population, but are probably not confounders*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes

2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	Yes
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	No
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	No
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes

	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes